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10/810,109	03/26/2004	Jean Francois Bach	IVD 938-2	8031

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EXAMINER	
HISSONG, BRUCE D	

ART UNIT	PAPER NUMBER
1646	

NOTIFICATION DATE	DELIVERY MODE
06/13/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/810,109	BACH ET AL.	
	Examiner	Art Unit	
	Bruce D. Hissong, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-4,6-15 and 17-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-4,6-15 and 17-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

1. The Applicants' response to the office action mailed on 5/17/2006, including arguments/remarks and amendments to the claims and specification, was received on 11/16/2006 and has been entered into the record.

2. Applicants' submission on 12/04/2006 of the Assignee showing of ownership per 37 CFR 3.73(b) is acknowledge and has been entered into the record.

3. The Applicants have added new claims 20-21. Therefore, claims 2-4, 6-15, and 17-21 are currently pending and are the subject of this office action.

Specification

Objection to the specification for containing bibliographic data that is inconsistent with the bibliographic data sheet, as set forth on page 2 of the office action mailed on 5/17/2006, is *withdrawn* in response to Applicants' amendments to the first paragraph of the specification to update the current bibliographic data.

Claim Objections

Objections withdrawn

1. Objection to claims 7 and 11, as set forth on page 2 of the office action mailed on 5/17/2006, is withdrawn in response to Applicants' amendments to the claims to recite "said lymphocytes autologous or syngeneic to the patient".

2. Objection to claim 14, as set forth on page 2 of the office action mailed on 5/17/2006, *withdrawn* in response to Applicants' amendments to the claim to recite "wherein said autoimmune disease is insulin-dependent diabetes mellitus."

3. Objection to claim 4, as set forth on page 3 of the office action mailed on 5/17/2006, is *withdrawn* in response to Applicants' amendments to the claim to recite "autoimmune-type".

4. Objection to claims 2-4 for being duplicates of claim 17, as set forth on page 3 of the office action mailed on 5/17/2006, is withdrawn in response to Applicants' arguments that claims 2-4 further limit the type of etiology or type of autoimmune disease to be treated.

Objections maintained/necessitated by amendment

5. The Examiner suggests the syntax of claim 7 can be improved by amending the claim to recite "said thymocytes being autologous or syngeneic to the patient.....".

6. Claims 7-9 remain objected to as being substantial duplicates of claim 10, as set forth on page 3 of the office action mailed on 5/17/2006. In the response received on 11/16/2006, the Applicants argue that claims 7-9 are drawn to a pharmaceutical composition, and claim 11 is drawn to a process, and therefore claims 7-9 cannot be duplicates of claim 11. It is noted that claim 11 was inadvertently mentioned in the last line of the objection. However, the objection clearly stated that claims 7-9 were objected to as being duplicates of claim 10. Therefore, for reasons of record set forth in the previous action, the objection is maintained.

7. Claims 12-13 remain objected to as being substantial duplicates of claim 14, as set forth on page 3 of the office action mailed on 5/17/2006. In the response received on 11/16/2006, the Applicants argue that the claims are not duplicates because, depending on the etiology of the disease, certain considerations might arise due to the dependence of the composition on the manner used to produce it. For example, a composition might be clinically acceptable in some situations, but not in other situations. Therefore, claims 12 and 13 cannot be duplicates of claim 14.

These arguments have been fully considered and are not persuasive. Regardless of the different limitations of each claim, the process steps of preparing each composition would be the same.

Claim Rejections - 35 USC § 112, first paragraph – enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-4, 6-15, and 17-19 *remain rejected*, and new claims 20-21 are also rejected, under 35 USC § 112, first paragraph, regarding lack of enablement for a method of treating any autoimmune disease other than insulin-dependent diabetes mellitus (IDDM), compositions for treating any autoimmune disease other than IDDM, or a process for preparing a composition for treating any autoimmune disease other than IDDM, as set forth on pages 3-5 of the prior office action mailed on 5/17/2006.

In the response received on 11/16/2006, the Applicants argue that claims 7, 11, and 17 are amended to include autoimmune diseases that arise from failure of immunoregulation by CD4+ cells or failure of production of IL-4.

This argument has been fully considered and is not persuasive. The Examiner notes that the claims have also been amended to recite methods comprising administration of T lymphocytes selected from the group consisting of thymocytes, wherein said thymocytes have been incubated in the presence of interleukin (IL)-7. However, this amendment alone does not sufficiently narrow the broad scope of the claims so that they are now enabled. As set forth in the previous office action, the specification is enabling for a method of treating IDDM, wherein said method comprises administration of thymocytes incubated in the presence of IL-7, but is not enabled for treatment of all possible autoimmune diseases. As currently amended, the claims still read on methods of treating, or compositions for treating, a large number of possible autoimmune disease. The claims are drawn to a method of treating autoimmune diseases that arise from failure of immunoregulation by $CD4^+$ cells. It is well-known in the art that $CD4^+$ cells regulate many facets of the immune response, and therefore almost any autoimmune disease can be considered as resulting from the failure of some type of immunoregulation by $CD4^+$ cells.

Thus, the claims read on a method of treating any autoimmune diseases resulting from deficient IL-4 production, and also autoimmune diseases that arise from other types of failed $CD4^+$ cell immunoregulation. The specification provides guidance and examples showing that IDDM can be treated by administration of thymocytes incubated in the presence of IL-7, but does provide any guidance or examples showing that any other type of autoimmune disease can be treated by this method. Furthermore, it is known in the art that not all autoimmune diseases arise from a deficiency in IL-4 production. For example, IL-4 appears to play an important role in the pathogenesis of disease in the NZB/NZW murine model of systemic lupus erythematosus (SLE), as anti-IL-4 neutralizing antibodies have been shown to prevent production of IgG autoantibodies, and also in preventing the disease (Nakajima *et al*, *J. Immunol.* 1997, Vol. 158, p. 1466-1472). Thus, a person of ordinary skill in the art would not be able to predict the effectiveness of the claimed method for treating diseases such as SLE that arise from a failure of immuoregulation by $CD4^+$ cells, but not from a deficiency in IL-4 production. A skilled artisan would therefore require further, undue experimentation to practice the claimed method for treatment of all possible autoimmune disorders.

Furthermore, because one of ordinary skill in the art would not be able to practice the claimed method for treating all possible autoimmune disorders resulting from failed immunoregulation by $CD4^+$ cells, a skilled artisan would also not be able to predict how to make and use a composition for the treatment of all possible autoimmune diseases, and would not know how to make and use a process for preparing a composition for treatment of all possible autoimmune diseases.

In summary, the breadth of the claims is still excessive because the claims read on all possible autoimmune diseases arising from a failure of immunoregulation by $CD4^+$ cells. The specification provides guidance and examples showing that IDDM can be treated by administration of thymocytes incubated in the presence of IL-7, but is not enabling for treatment of all possible autoimmune diseases arising as a result of failure of immunoregulation of $CD4^+$ cells. Therefore, a person of ordinary skill in the art would require further, undue experimentation in order to make and use a method, composition, or process of preparing a composition, for treatment of any autoimmune disease other than IDDM.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Rejections withdrawn

1. Rejection of claims 3, 9, and 13 under 35 USC § 112, second paragraph, for being indefinite regarding the phrase "quantitative and functional deficiency of a T cell", as set forth on page 6 of the prior office action mailed on 5/17/2006, is withdrawn in response to Applicants' amendments to the claims to delete the phrase.

2. Rejection of claim 4 under 35 USC § 112, second paragraph, for being indefinite regarding the phrase "autoimmune type pathogenic mechanisms in a therapy associated with treating AIDS", as set forth on page 6 of the prior office action mailed on 5/17/2006, is withdrawn in response to Applicants' amendments to the claim to delete the phrase.

3. Rejection of claim 2-4, 6-15, and 17-19 under 35 USC § 112, second paragraph, for missing essential method steps, as set forth on pages 5-6 of the prior office action mailed on 5/17/2006, is withdrawn in response to Applicants' amendments to the claims to recite incubation of thymocytes in a "therapeutically effective dose" of IL-4.

Rejections maintained/necessitated by amendment

3. Claims 2-4, 6-15, and 17-21 are *rejected* under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are drawn to a method comprising incubation of thymocytes in IL-7, at a therapeutically effective dose "effecting IL-4 production". The claims are indefinite because the claims do not state the degree or type of "effecting" IL-4 production in the claimed method, and thus the metes and bounds of "effecting IL-4 production" are not clear.

4. Claims 2-4, 6-15, and 17-21 are *rejected* under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite autoimmune diseases "related to a failure of immunoregulation of $CD4^+$ cells". The metes and bounds of this term are unclear because

the type or degree of immunoregulation is not defined by the claims or the specification, and therefore could encompass virtually any biological activity attributed to a $CD4^+$ cell.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Rejections maintained:

1. Claims 2-4, 15, and 17 *remain rejected* under 35 USC § 102(e) as being anticipated by Grabstein *et al* ("Grabstein" - US 5,681,557, as set forth on pages 6-7 of the office action mailed on 5/17/2006. In the response received on 11/16/2006, the Applicants argue that Grabstein does not anticipate the claims of the instant invention because as currently amended, the claims recite an end-point of increased IL-4 production. The Applicants assert that Grabstein does not teach increased IL-4 production, and therefore does not meet this limitation.

This argument has been fully considered and is not persuasive. The currently amended claims recite an end-point of an effective dose "effecting" IL-4 production. As stated in above in the rejection under 35 U.S.C. 112, 2nd paragraph, the metes and bounds of "effecting IL-4 production" are not clear. Although Grabstein does not specifically recite IL-4 production, it would be expected, in the absence of evidence to the contrary, that the method of IL-7 administration taught by Grabstein would "effect" IL-4 production in some way. Therefore, for these reasons and those set forth in page 7 of the office action mailed on 5/17/2006, Grabstein meets the limitations of the claims of the instant invention.

2. Claims 2-4, 15, and 17 *remain rejected* under 35 USC § 102(b) as being anticipated by Williams *et al* ("Williams – US 5,032,396), as set forth on pages 7-8 of the office action mailed on 5/17/2006. In the response received on 11/16/2006, the Applicants argue that

Williams does not anticipate the claims of the instant invention because as currently amended, the claims recite an end-point of increased IL-4 production. The Applicants assert that Williams does not teach increased IL-4 production, and therefore does not meet this limitation.

This argument has been fully considered and is not persuasive. The currently amended claims recite an end-point of an effective dose "effecting" IL-4 production. As stated in above in the rejection under 35 U.S.C. 112, 2nd paragraph, the metes and bounds of "effecting IL-4 production" are not clear. Although Williams does not specifically recite IL-4 production, it would be expected, in the absence of evidence to the contrary, that the method of IL-7 administration taught by Williams would "effect" IL-4 production in some way. Therefore, for these reasons and those set forth in pages 7-8 of the office action mailed on 5/17/2006, Williams meets the limitations of the claims of the instant invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2-3, 6-15, and 17-19 *remain rejected*, and new claims 20-21 are also rejected, under 35 USC § 103(a) as being obvious in view of the combination of Gombert *et al* ("Gombert") and Jicha *et al* ("Jicha"), as set forth on pages 8-9 of the office action mailed on 5/17/2006.

In the response received on 11/16/2006, the Applicants argue that Gombert is not properly cited as prior art against the present application because the reference was published after the claimed priority date, as set forth in the International Search Report. Furthermore, the Applicants note that Marc Gombert and Andre Herbelin are authors of the cited reference, and are also inventors listed on the instant application. The Applicants assert that therefore the reference is not evidence of invention by another.

These arguments have been fully considered and are not persuasive. It is noted that the instant application is a 371 of PCT/FR97/00343, filed on 2/26/1997, and claims foreign priority to FR 96 02501, filed on 2/28/1996. Gombert has an electronic publication date of 2/1/1996, and

therefore, Gombert is in fact proper prior art over the instant application. Furthermore, it is noted that in addition to inventors Gombert, Herbelin, and Bach, the Gombert reference lists 4 other authors that are not listed as inventors in the instant invention. Thus, the inventive entity of the instant application is distinct from the authors of the Gombert reference, and therefore the Gombert reference is indeed evidence of invention by another. The Examiner suggests submission of an affidavit under 37 CFR 1.131 may overcome this rejection. Alternatively, the rejection may also be overcome by an affidavit under 37 CFR 1.132 showing that the additional authors of the Gombert reference did not invent the currently claimed subject matte.

For these reasons, and the reasons set forth on pages 8-9 of the office action mailed on 5/17/2006, claims 2-3, 6-15, and 17-19 are obvious in view of the combination of Gombert and Jichi. Furthermore, new claims 20-21, which are drawn to methods of treatment comprising administering an effective dose of T cells incubated in the presence of IL-7, said effective dose effecting IL-4 production, are also obvious in view of the combined teachings of Gombert and Jicha. As stated in the previous office action, Gombert teaches that a subset of thymocytes is capable of IL-4 secretion, and this IL-4 secretion is impaired in the murine model of diabetes. Incubation of this subset restores the ability to secrete IL-7. Jicha teaches a method of adoptive immunotherapy comprising administration of T cell incubated with IL-7. Thus, because Gombert provides the motivation for treating thymocytes with IL-7 to restore IL-4 production in diabetes patients, and Jicha teaches methods of administering IL-7 treated cells, a person of ordinary skill in the art would have both the motivation, and a reasonable expectation of success, in using the method of Jicha to administer IL-7-treated thymocytes to restore IL-4 production in diabetes.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re*

Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1. Claims 2-4, 15, and 17 *remain rejected* on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of US 6,713,053. In the response received on 11/16/2006, the Applicants have deferred addressing this rejection until the identification of allowable subject matter.

2. Claims 2-4, 7-15, and 17-19 *remain rejected*, and new claims 20-21 are also rejected, on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of US 6,713,053, in view of Jicha *et al.* In the response received on 11/16/2006, the Applicants have deferred addressing this rejection until the identification of allowable subject matter.

Conclusion

No claim is allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571) 272-3324. The examiner can normally be reached M-F from 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BDH
Art Unit 1646

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